FILE 'CAPLUS, WPIDS, MEDLINE' ENTERED AT 13:42:39 ON 26 AUG 2003

L1 88430 S (PHOTODYNAM? OR PROPHYRIN? OR METALLOPORPHYRIN? OR ROSE BENGA
L2 220998 S L1 OR ANTHRACENE OR HYPERICIN OR METHYLCHOLANTHRENE OR NEUTRA
L3 774355 S CORONARY OR INFARCTION OR MYOCARDIAL OR ARTERIOSCLEROSIS OR H
L4 716 S L2 (25A) L3
L5 538 DUP REM L4 (178 DUPLICATES REMOVED)
L6 2 S L5 AND (QUINONE# OR BENZOQUINONE# OR NAPHTHOQUINONE# OR CYCL
L7 536 S L5 NOT L6

FILE 'STNGUIDE' ENTERED AT 13:52:56 ON 26 AUG 2003

FILE 'CAPLUS, WPIDS, MEDLINE' ENTERED AT 14:18:11 ON 26 AUG 2003
L8 13 S L7 AND (OZON? OR PEROXID? OR GERANIOL OR TERPINEOL OR CITRON

=> d que l1; d que l2; d que l3; d que l6
L1 88430 SEA (PHOTODYNAM? OR PROPHYRIN? OR METALLOPORPHYRIN? OR ROSE BENGAL OR CHLOROPHYLLIN OR HEMIN OR CORRIN# OR TEXAPHRIN# OR METHYLENE BLUE OR HEMATOXYLIN OR EOSIN OR ERYTHROSIN OR LACTOFLAVIN)

Printed out in Back of this

L1 88430 SEA (PHOTODYNAM? OR PROPHYRIN? OR METALLOPORPHYRIN? OR ROSE BENGAL OR CHLOROPHYLLIN OR HEMIN OR CORRIN# OR TEXAPHRIN# OR METHYLENE BLUE OR HEMATOXYLIN OR EOSIN OR ERYTHROSIN OR LACTOFLAVIN)
L2 220998 SEA L1 OR ANTHRACENE OR HYPERICIN OR METHYLCHOLANTHRENE OR NEUTRAL RED OR FLUORESCEIN#

L3 774355 SEA CORONARY OR INFARCTION OR MYOCARDIAL OR ARTERIOSCLEROSIS OR HEART DISEASE# OR ARTERIES

L1 88430 SEA (PHOTODYNAM? OR PROPHYRIN? OR METALLOPORPHYRIN? OR ROSE BENGAL OR CHLOROPHYLLIN OR HEMIN OR CORRIN# OR TEXAPHRIN# OR METHYLENE BLUE OR HEMATOXYLIN OR EOSIN OR ERYTHROSIN OR LACTOFLAVIN)
L2 220998 SEA L1 OR ANTHRACENE OR HYPERICIN OR METHYLCHOLANTHRENE OR NEUTRAL RED OR FLUORESCEIN#
L3 774355 SEA CORONARY OR INFARCTION OR MYOCARDIAL OR ARTERIOSCLEROSIS OR HEART DISEASE# OR ARTERIES
L4 716 SEA L2 (25A) L3
L5 538 DUP REM L4 (178 DUPLICATES REMOVED)
L6 2 SEA L5 AND (QUINONE# OR BENZOQUINONE# OR NAPHTHOQUINONE# OR CYCLOHEXADIENEDIONE OR (CYCLHEXADIENE (3A) DIONE))

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All Reviewed. Selected refs from L7 printed out on next pages

Nothing useful - Mostly for state of art & Background

=> d l7 30 33 44 55 57 89 103 128 129 182 197 209 214 234 273 279 281 284 375 bib ab

L7 ANSWER 30 OF 536 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:513875 CAPLUS
DN 136:82003
TI **Photodynamic** therapy with motexafin lutetium (Lu-Tex) reduces experimental graft **coronary** artery disease
AU Yamaguchi, Atsushi; Woodburn, Kathryn W.; Hayase, Motoya; Hoyt, Grant; Robbins, Robert C.
CS Departments of Cardiothoracic Surgery and Cardiovascular Medicine, Stanford University School of Medicine, Stanford, CA, 94305, USA
SO Transplantation (2001), 71(11), 1526-1532
CODEN: TRPLAU; ISSN: 0041-1337
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB Motexafin lutetium (Lu-Tex) is a photodynamic therapy (PDT) agent that localizes in atheromatous plaque in which it can be activated by farred light. Lu-Tex biolocalization was examd. in graft coronary artery disease (GCAD) with a rodent allograft model. After photoactivation, the effect on intimal proliferation was assessed. A PVG to ACI rat heterotopic heart transplantation model was used. Lu-Tex (10 mg/kg) was i.v. administered 90 days after transplantation. Photoactivation was performed 24 h after Lu-Tex administration. A light-emitting diode, central wavelength of 742 nm, was used to illuminate the i.p. placed allografts via a laparotomy (light fluence of 75 J/cm2 at a power d. of 75 mW/cm2). Animals were divided into four groups according to postoperative treatments: PDT with Lu-Tex injection and light illumination (n=21), Lu-Tex injection and laparotomy (n=14), laparotomy with light only (n=14), and laparotomy only (n=16). GCAD was quant. assessed 14 days after treatments. Lu-Tex localized in atherosclerotic plaque in vessels with GCAD. PDT significantly reduced both the percent of affected vessels and intimal proliferation compared to all other control study groups. .alpha.-Smooth muscle cell actin and anti-rat macrophage antibody-pos. areas were significantly reduced within the neointima in allografts treated with PDT compared to all other study groups. PDT significantly reduced atherosclerotic lesions of GCAD. Lu-Tex-mediated PDT may, therefore, be a potential method for treating accelerated atherosclerosis assocd. with transplantation.
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 33 OF 536 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:265274 CAPLUS
DN 134:262933
TI Significance of dosimetry in **photodynamic** therapy of injured **arteries**
IN Lamuraglia, Glenn Michael
PA The General Hospital Corporation Doing Business as Massachusetts General Hos, USA
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001024825	A2	20010412	WO 2000-US27140	20001002
WO 2001024825	A3	20020103		

W: CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
PRAI US 1999-157325P P 19991001

US 1999-157409P P 19991001
AB Photodynamic therapy (PDT), the light activation of methylene blue or benzoporphyrin derivs. to produce free-radicals, was shown in vivo to inhibit intimal hyperplasia (IH) and restenosis. An effective amt. of photosensitizer is delivered to the injured site in vivo and the site is irradiated with sufficient light energy between about 300 and 900 nm such that restenosis is modulated. The light source used is a laser and the light energy about 100 J/cm2. The present invention provides an effective clin. approach for PDT treatment which modulates the vascular intervention injury healing response.

L7 ANSWER 44 OF 536 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:691961 CAPLUS
DN 134:307299
TI **Photodynamic** therapy induces apoptosis in intimal hyperplastic **arteries**
AU LaMuraglia, Glenn M.; Schiereck, Jan; Heckenkamp, Joerg; Nigri, Giuseppe; Waterman, Peter; Leszczynski, Dariusz; Kossodo, Sylvie
CS Division of Vascular Surgery, Harvard Medical School, Boston, MA, 02114, USA
SO American Journal of Pathology (2000), 157(3), 867-875
CODEN: AJPAA4; ISSN: 0002-9440
PB American Society for Investigative Pathology
DT Journal
LA English
AB Photodynamic therapy (PDT) generates free radicals through the absorption of light by photosensitizers. PDT shows promise in the treatment of intimal hyperplasia, which contributes to restenosis, by completely eradicating cells in the vessel wall. This study investigates the mechanisms of PDT-induced cell death. Chloroaluminum-sulfonated phthalocyaninePDT, using the photosensitizer chloroaluminum-sulfonated phthalocyanine (1 mg/kg) and laser light (.lambda. = 675 nm) 100 J/cm2 was administered to rat carotid arteries after balloon injury-induced intimal hyperplasia. Apoptosis was detd. by cell morphol. with light microscopy and transmission electron microscopy, DNA cleavage by terminal dUTP nick-end labeling staining, and nucleosomal fragmentation (ladder pattern) by DNA agarose gel electrophoresis. Four hours after PDT, apoptosis was obsd. in vascular cells, as evidenced by terminal dUTP nick-end labeling staining and transmission electron microscopy. Within 24 h no cells were present in the neointima and media. Immunofluorescence using an .alpha.-smooth muscle cell actin antibody confirmed the disappearance of all neointimal and medial cells within 24 h. No inflammatory cell infiltrate was obsd. during this time frame. Apoptosis was sharply confined to the PDT treatment field. These data demonstrate that vascular PDT induces apoptosis as a mechanism of rapid, complete, and precise cell eradication in the artery wall. These findings and the lack of inflammatory reaction provide the basis for understanding and developing PDT for a successful clin. application in the treatment of hyperplastic conditions such as restenosis.
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 55 OF 536 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:161288 CAPLUS
DN 132:202301
TI Preparation of metalloporphyrin and porphyrin derivatives, their use in photodynamic therapy and medical devices containing them
IN Love, William Guy; Cook, Michael John; Russell, David Andrew
PA Destiny Pharma Limited, UK; University of East Anglia
SO PCT Int. Appl., 131 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000012512	A1	20000309	WO 1999-GB2864	19990831
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2341507	AA	20000309	CA 1999-2341507	19990831
	AU 9956360	A1	20000321	AU 1999-56360	19990831
	EP 1107971	A1	20010620	EP 1999-943075	19990831
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002523509	T2	20020730	JP 2000-567534	19990831
PRAI	GB 1998-18789	A	19980828		
	GB 1999-12971	A	19990604		
	WO 1999-GB2864	W	19990831		

OS MARPAT 132:202301

AB Metalloporphyrins (I) are prepd., wherein R1, R2, R3, R4, R5, R6, R7, R8, R9 and X have meanings given in the description and Y1, Y2 and Y3 are either absent or represent O, Z is absent or represents lower alkylene, M is a metal or metalloid and A-B and C-D are independently CH:CH or CH2CH2, which are useful in the treatment of medical conditions for which a photodynamic compd. is indicated. Compns., app. and methods of treatment of a medical condition for which a photodynamic compd. is indicated are also disclosed. Thus, {5,5'-{4,4'-[12,12'-dithiobis(dodecyloxy)phenyl]}-10,10',15,15',20,20'-hexakis(3,4,5-tridecyloxyphenyl)diporphyrinato}zinc was prepd. and deposited on the surface of a gold coated vascular stent for use in photodynamic therapy.

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 57 OF 536 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:94156 CAPLUS
DN 132:248011
TI Texaphyrins. New drugs with diverse clinical applications in radiation and photodynamic therapy
AU Sessler, J. L.; Miller, R. A.
CS Department of Chemistry & Biochemistry, University of Texas, Austin, TX, USA
SO Biochemical Pharmacology (2000), 59(7), 733-739
CODEN: BCPCA6; ISSN: 0006-2952
PB Elsevier Science Inc.
DT Journal; General Review
LA English
AB A review with 42 refs. The texaphyrins are quintessential metal-coordinating expanded porphyrins constitute a new series of synthetic porphyrin analogs that show promise as drugs for use in a range of medical therapies. Currently, two different water-solubilized lanthanide(III) texaphyrin complexes, namely the gadolinium(III) and lutetium(III) derivs. 1 and 2 (Gd-Tex and Lu-Tex, resp.), are being tested clin. The first of these, XCYTRIN, is in a pivotal Phase III clin. trial as a potential enhancer of radiation therapy for patients with metastatic cancers to the brain receiving whole brain radiation therapy. The second, in various formulations, is being tested as a photosensitizer for use in: (i) the **photodynamic** treatment of recurrent breast cancer LUTRIN; Phase II clin. trials complete, (ii) photoangioplastic redn. of atherosclerosis involving peripheral **arteries** ANTRIN; now in Phase II testing, and (iii) light-based treatment of age-related macular degeneration OPTRIN; currently in Phase I clin. trials, a

vision-threatening disease of the retina. Taken in concert, these two metallotexaphyrins provide a powerful new class of exptl. drugs whose diverse potential utility is abetted by a combination of well-optimized phys. features, favorable tissue biolocalization characteristics, and novel mechanisms of action. Interestingly, these mechanisms may alter conventional wisdom regarding mechanisms of radiation therapy and the pathophysiol. of atherosclerosis.

RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 89 OF 536 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:173920 CAPLUS
DN 128:267763
TI Importance of the treatment field for the application of vascular photodynamic therapy to inhibit intimal hyperplasia
AU van Eps, Randolph G. Statius; ChandraSekar, N. R.; Hasan, Tayyaba; Lamuraglia, Glenn M.
CS Division of Vascular Surgery of the General Surgical Services, Wellman Laboratories of Photomedicine, MA, USA
SO Photochemistry and Photobiology (1998), 67(3), 337-342
CODEN: PHCBAP; ISSN: 0031-8655
PB American Society for Photobiology
DT Journal
LA English
AB Intimal hyperplasia (IH) plays a dominant role in the development of restenosis. In previous studies, photodynamic therapy (PDT) prevented IH induced by segmental balloon injury of the rat carotid. The crit. elements required to control IH effectively with this technique are not fully understood. This study assessed the importance of the treatment field by studying the repair process of injured vessels, in which the PDT-treatment field did not target the entire injured area. The entire rat common carotid artery was balloon-injured to induce IH, whereas only the cervical segment below the bifurcation was subjected to PDT by external light irradn. after administration of the photosensitizer chloroaluminum sulfonated phthalocyanine. Light irradn. of injured arteries without photosensitizer served as control for PDT, and PDT of uninjured arteries was included as a control group for the balloon injury. Histol. characterization of the repair process was sequentially assessed. Balloon-injured arteries without PDT displayed rapid IH development with a peak at 2 wk. **Photodynamic** therapy of balloon-injured **arteries** resulted in complete local depletion of medial smooth muscle cells (SMC), which was assocd. with a lack of IH until 2 wk. However, at 4 and 16 wk there was significant IH in PDT-treated arteries despite a lack of medial SMC repopulation. A wave of IH progression over the acellular media was obsd. in these arteries, migrating from the injured non-PDT-treated area. The PDT of uninjured arteries did not result in IH and was also assocd. with a persistent acellular media. Delayed IH development after PDT of injured vessels can result from IH progression from an injured site not included in the treatment field. This also indicated that the source of cells developing the intimal hyperplasia lesion can originate from an area remote from the lesion. Together with previous results and the detn. that PDT itself does not induce IH, it can be reasoned that inclusion of the whole injured artery or a section of an uninjured margin in the treatment field is essential for effective PDT prevention of IH.

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 103 OF 536 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:319963 CAPLUS
DN 126:327524
TI Delivery of benzoporphyrin derivative, a photosensitizer, into atherosclerotic plaque of Watanabe heritable hyperlipidemic rabbits and balloon-injured New Zealand rabbits

AU Allison, B. A.; Crespo, M. T.; Jain, A. K.; Richter, A. M.; Hsiang, Y. N.; Levy, J. G.
CS Department of Surgery, University of British Columbia, Vancouver, BC, V6T 2B5, Can.
SO Photochemistry and Photobiology (1997), 65(5), 877-883
CODEN: PHCBAP; ISSN: 0031-8655
PB American Society for Photobiology
DT Journal
LA English
AB In this study we compared the plasma distribution and arterial accumulation of a photosensitizer, benzoporphyrin deriv. (BPD) monoacid ring A, in two models of atherosclerosis: the spontaneous lesions of the Watanabe heritable hyperlipidemic (WHHL) rabbit and induced lesions of the balloon-injured, cholesterol-fed New Zealand white (NZW) rabbit. Selective uptake and retention of a photosensitizer by the abnormal portion of a vessel is a necessity in order for **photodynamic** therapy to become a successful modality for inhibition of intimal hyperplasia, selective removal of atherosclerotic tissue or imaging of diseased **arteries**. Liposome-based formulations were compared to freshly isolated native low d. lipoprotein (LDL) and acetylated-LDL (Ac-LDL) as delivery vehicles for BPD. Plasma distribution of the photosensitizer was analyzed by KBr d. gradient ultracentrifugation. Although the delivery vehicle influenced plasma distribution immediately postinjection, BPD subsequently partitioned according to the plasma concn. of the lipoproteins. Photosensitizer level in plaque and normal artery specimens was detd. by Et acetate extn. and spectrofluorometric measurement. The measurement of BPD in normal and atherosclerotic arterial tissue demonstrated a selective accumulation in atherosclerotic tissue. Preassocn. with LDL and Ac-LDL enhanced accumulation of BPD in atherosclerotic tissue when compared with normal artery (mean ratios of 2.8 and 4.1 were achieved, resp.). These results indicate that the preferential uptake of BPD by atherosclerotic plaque can be enhanced by preassocn. with plasma lipoproteins, suggesting that light activation could lead to a highly selective destruction of diseased vascular tissue.

L7 ANSWER 128 OF 536 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:741983 CAPLUS
DN 123:192532
TI The effect of **photodynamic** therapy on the mechanical integrity of normal rabbit carotid **arteries**
AU Grant, W. E.; Buonaccorsi, G.; Speight, P. M.; MacRobert, A. J.; Hopper, C.; Bown, S. G.
CS Department of Surgery, University College London Medical School, London, UK
SO Laryngoscope (1995), 105(8, Pt. 1), 867-71
CODEN: LARYA8; ISSN: 0023-852X
PB American Laryngological, Rhinological and Otological Society, Inc.
DT Journal
LA English
AB Photodynamic therapy (PDT) for tumor ablation is effective in the treatment of superficial cancers. Adjunctive intraoperative PDT has been proposed for the "sterilization" of tumor beds after the resection of malignancies. Arteries in photosensitized animal models exposed to appropriate light receive characteristic injury. This study was conducted to det. whether photodynamic injury to the rabbit carotid artery results in thrombotic occlusion or weakening of the vessel wall. PDT of the carotid arteries of New Zealand white rabbits, using either disulfonated aluminum phthalocyanine or 5-aminolevulinic-acid-induced protoporphyrin IX as the photosensitizer, was performed with a light dose of 100 J/cm2. Histol. examn. of the carotids treated with either agent demonstrated typical full-thickness loss of cellularity 3 days after PDT. All vessels remained patent, and no inflammatory infiltrate was evident. Elastin van Gieson staining showed preservation of inner and medial elastic laminae and medial and adventitial collagen. Addnl. rabbits were similarly

treated with PDT to 1-cm segments of both common carotid arteries. The animals were sacrificed at 3, 7, and 21 days. The carotids were exposed, and both control and treated segments were subjected to intraluminal hydrostatic distention until the vessels burst. No redn. in the pressure required to burst the vessels was evident in the treated vessels as compared with the control vessels. The authors of the study concluded that despite full-thickness cell death, PDT-treated arteries are not at risk for thrombotic occlusion or hemorrhage.

L7 ANSWER 129 OF 536 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:702859 CAPLUS
DN 123:164182
TI Local delivery of photosensitizing drugs in **arteries**: a novel approach to **photodynamic** therapy for the prevention of intimal hyperplasia
AU Adili, Farzin; van Eps, Randolph G. S.; LaMuraglia, Glenn M.
CS Harvard Medical School, Massachusetts General Hospital, Boston, MA, 02114, USA
SO Proceedings of SPIE-The International Society for Optical Engineering (1995), 2395, 402-8
CODEN: PSISDG; ISSN: 0277-786X
DT Journal
LA English
AB The long-term benefit of coronary or peripheral vascular interventions is limited by restenosis, due to intimal hyperplasia (IH). Photodynamic therapy (PDT) with systemic delivery of the photosensitizing drug, performed either at the time or shortly after vascular injury, has been demonstrated to effectively inhibit the development of exptl. IH. However, in order to deliver large quantities of the photosensitizer, but avoid systemic photosensitization, local delivery of the drug appears to be an advantageous option. An exptl. model was therefore developed to deliver benzporphyrin deriv. (BPD-MA) directly into isolated segments of balloon-injured rat common carotid arteries, and to study the uptake in serum and arterial tissue by means of spectrofluorometry. Furthermore, early effects of local vs. systemic drug delivery and subsequent PDT treatment, were investigated with light microscopy and morphometric anal. Local delivery of BPD lead to effective drug concns. in the artery with complete depletion of endothelial and smooth muscle cells, already 24 h after PDT. The media appeared compacted and acellular. No thrombosis or occlusion were obsd. Serum concns. of BPD, after local delivery, were at the detection threshold, whereas systemic application resulted in significantly higher serum but equiv. tissue drug concns. In conclusion, these data demonstrate that local delivery of BPD results in tissue concns., appropriate to perform an efficient vascular PDT treatment of the arterial wall.

L7 ANSWER 182 OF 536 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1993:116775 CAPLUS
DN 118:116775
TI Pharmaceuticals for treatment of active oxygen-induced injury
IN Namiki, Mitsuo; Nakamura, Kunie
PA Namiki, Mitsuo, Japan; Nakamura, Kunie
SO Jpn. Kokai Tokkyo Koho, 3 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 04327534	A2	19921117	JP 1991-187123	19910424
PRAI JP 1991-187123		19910424		

AB Pharmaceuticals, useful for therapeutic and propylactic treatment of active O-induced injury (e.g. **arteriosclerosis**, nephritis, diabetes, etc.), contain Fe **chlorophyllin** as an active

ingredient. Fe chlorophyllin Na salt inhibited active O formation in a hypoxanthine system with IC50 of 2.90 .mu.g/mL.

L7 ANSWER 197 OF 536 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1992:51577 CAPLUS
DN 116:51577
TI The use of synthetic metalloporphyrins in the treatment of hypertension and other vascular disorders
IN Levere, Richard D.; Abraham, Nader G.; Schwartzman, Michel L.; Kappas, Attallah
PA Rockefeller University, USA
SO PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9116053	A1	19911031	WO 1991-US2657	19910418
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
	AU 9177555	A1	19911111	AU 1991-77555	19910418
PRAI	US 1990-513751		19900424		
	WO 1991-US2657		19910418		

AB High vascular resistance disorders of mammals are treated by administration of a sufficient amt. of a synthetic metalloporphyrin with heme oxygenase-inducing activity. Treatable disorders include e.g. hypertension, vasospasm, angina pectoris, cerebral ischemia, and preeclampsia. Administration of Co protoporphyrin to spontaneous hypertensive rats lowered blood pressure and cytochrome P 450 levels; changes in enzymic activities are also reported.

L7 ANSWER 209 OF 536 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1991:400479 CAPLUS
DN 115:479
TI Pharmacological studies of arrhythmias induced by rose bengal photoactivation
AU Bernier, Michele; Kusama, Yoshiki; Borgers, Marcel; Ver Donck, Luc; Valdes-Aguilera, Oscar; Neckers, Douglas C.; Hearse, David J.
CS Rayne Inst., St. Thomas' Hosp., London, SE1 7EH, UK
SO Free Radical Biology & Medicine (1991), 10(5), 287-96
CODEN: FRBMEH; ISSN: 0891-5849
DT Journal
LA English
AB Singlet oxygen and superoxide prodn. by rose bengal photoactivation leads to rapid electrophysiol. changes and arrhythmias. To investigate which intermediate is causative and to probe possible mechanisms, hearts controls, all or most hearts exhibited ventricular premature beats, ventricular tachycardia, and complete atrioventricular block. Most antioxidants tested had no protective effect; histidine, however, delayed the onset of electrocardiog. (ECG) changes. In further studies, two antiarrhythmic agents (quinidine and verapamil) had no or little protective effect, whereas R56865 delayed the onset of ECG changes and reduced the incidence of arrhythmias. However, spectrophotometric and laser pulse radiolysis studies showed that this apparent protective effect might have resulted from an interaction between R56865 and the rose bengal mol., leading to a redn. in singlet oxygen prodn. In conclusion, the electrophysiol. changes induced by rose bengal photoactivation are likely to be due to single oxygen; antiarrhythmic drugs appear to be unable to protect against the injury unless there is some interaction with the photoactivation process.

L7 ANSWER 214 OF 536 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1991:199406 CAPLUS

DN 114:199406
TI Study of the vasodilating activity of salbutamol on dog **coronary arteries**. Unexpected effects of **methylene blue**
AU Bernard, Florence; Jouquey, Simone; Hamon, Gilles
CS Cent. Rech. Roussel-Uclaf, Romainville, F-93230, Fr.
SO Pharmacology (1991), 42(5), 246-51
CODEN: PHMGBN; ISSN: 0031-7012
DT Journal
LA English
AB The vascular relaxant effect of salbutamol and its dependence on the endothelium were studied in the isolated dog coronary artery, precontracted with prostaglandin F2.alpha.. Salbutamol induced a concn.-dependent relaxation which was partially inhibited by removal of endothelial cells. Atenolol 10-6 mol/L, a .beta.1-selective antagonist, inhibited the relaxant effect of salbutamol both in the presence and in the absence of endothelium. Conversely, ICI 118,551 10-6 mol/L, a .beta.2-selective antagonist, antagonized the response to salbutamol only in intact vessels. Methylene blue amplified markedly the relaxation to salbutamol but only in denuded rings. Therefore, the vasodilating effect of salbutamol on large coronary arteries seems to result from the stimulation of both, .beta.1-receptors on smooth muscle cells and .beta.2-receptors on endothelial cells, demonstrating the existence of the two types of adrenoceptors in the wall of large dog coronary arteries. In addn., the effect obtained with methylene blue in this study shed some doubts on its specificity as a guanylate cyclase inhibitor.

L7 ANSWER 234 OF 536 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1988:466633 CAPLUS
DN 109:66633
TI Inhibition of vasodilatation by **methylene blue** in large and small **arteries** of the dog hindlimb in vivo
AU Sobey, C. G.; Woodman, O. L.; Dusting, G. J.
CS Dep. Physiol., Univ. Melbourne, Parkville, Australia
SO Clinical and Experimental Pharmacology and Physiology (1988), 15(5), 401-10
CODEN: CEXPB9; ISSN: 0305-1870
DT Journal
LA English
AB Injection of acetylcholine (ACh, 0.0005-2 .mu.g/kg) or glyceryl trinitrate (GTN, 0.1-20 .mu.g/kg) into the femoral artery increased the artery diam., femoral blood flow, and heart rate and reduced femoral vascular resistance and systemic arterial blood pressure in anesthetized dogs. The i.v. injection of ACh (2 .mu.g/kg) produced a small decrease in systemic arterial pressure and an increase in heart rate, but did not dilate the hindlimb vessels. Methylene blue, a guanylate cyclase inhibitor, continuously infused into the femoral artery (10 mg/min), attenuated the increase in femoral artery diam. and femoral blood flow, and the decrease in femoral vascular resistance produced by intra-arterial injections of both ACh and GTN. In addn., methylene blue potentiated the decrease in systemic arterial pressure produced by ACh. These results suggest that both ACh- and GTN-induced vasodilation in vivo occurs through a mechanism involving guanylate cyclase activation in large arteries and resistance vessels in the dog hindlimb. Methylene blue inhibited the local vasodilator actions of ACh in the femoral vasculature despite potentiating the systemic depressor response to that agent.

L7 ANSWER 273 OF 536 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1967:420449 CAPLUS
DN 67:20449
TI **Methylene blue**, a short acting inhibitor of monoamine oxidase, in the therapy of **myocardial** infarcts
AU Pick, K.
CS I. Innere Abt. Krankenhauses, Prague, Czech.
SO Abhandlungen der Deutschen Akademie der Wissenschaften zu Berlin, Klasse

fuer Medizin (1966), (2), 307-9
CODEN: ADWMAX; ISSN: 0568-4250
DT Journal
LA German
AB **Methylene blue** (I) is effective in **myocardial infarction**. Of 96 such cases, 57 patients were treated with I while the other 39 formed the control group. I, 100 mg., was administered in 20% glucose or physiol. soln. by i.v. injection at intervals of 12 hrs. for 10-14 days. This treatment was well tolerated. All patients later had the usual anticoagulant therapy. In half the cases treated, a significant decrease in angina pain could be brought about after 10-15 min. No marked fluctuations in blood pressure were observed in patients being treated with I as compared with the control group. Prothrombin time was regularly reduced and no thromboembolisms of the peripheral vascular system were found, while in the control group 4 such complications occurred. Coupled with its sedative-analgetic action, I may be used in prophylactic therapy.

L7 ANSWER 279 OF 536 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1938:45435 CAPLUS
DN 32:45435
OREF 32:6329h
TI The influence of vasodilators in experimental **coronary** occlusion and the action of **methylene blue** on blood vessels
AU Addarii, F.; Freundlich, J.
SO Archiv fuer Experimentelle Pathologie und Pharmakologie (1937), 185, 525-38
CODEN: AEXPBL; ISSN: 0365-2041
DT Journal
LA Unavailable
AB Unavailable

L7 ANSWER 281 OF 536 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2003-103676 [09] WPIDS
DNN N2003-082694 DNC C2003-026334
TI Use of metallated porphyrin for treating or detecting diseases of cardiovascular system in combination with irradiation.
DC A96 B02 S03 S05
IN GREENE, S; LEITCH, I M; ROBINSON, B C; RYCHNOVSKY, S
PA (GREE-I) GREENE S; (LEIT-I) LEITCH I M; (ROBI-I) ROBINSON B C; (RYCH-I) RYCHNOVSKY S; (MIRA-N) MIRAVANT PHARM INC
CYC 100
PI WO 2002096366 A2 20021205 (200309)* EN 247p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW
US 2003105069 A1 20030605 (200339)
ADT WO 2002096366 A2 WO 2002-US17180 20020531; US 2003105069 A1 Provisional US 2001-295345P 20010531, US 2002-159005 20020531
PRAI US 2001-295345P 20010531; US 2002-159005 20020531
AB WO 200296366 A UPAB: 20030407
NOVELTY - Use of a metallated porphyrin (I) is claimed for treating or detecting diseases of the cardiovascular system by administering (I) that coordinates a metal in the central pyrrolic core and irradiating (I) with energy at a wavelength capable of exciting the molecule to give the desired detection or therapeutic effect.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) use of a tetrapyrrolic macrocycle (II) comprising a porphyrin, an azaporphyrin, a diazaporphyrin, a triazaporphyrin, a corrole, a porphycene, an isoporphycene, a hemiporphycene or a corrphycene, that

coordinates gallium in the central pyrrolic core for treating or detecting diseases of the cardiovascular system;

(2) restructuring the epithelial or endothelial layers of skin or stopping or arresting hair growth which comprises topically or systemically administering a tetrapyrrolic molecule that coordinates gallium in the central tetrapyrrolic core and irradiating the molecule with energy at a wavelength capable of exciting the molecule;

(3) use of a gallium tetrapyrrole molecule for detecting or treating tissue which comprises locally, systemically, intramuscularly or intraperitoneally administering a gallium tetrapyrrolic molecule and irradiating the molecule with energy at a wavelength capable of exciting the molecule, where the tissue belongs to the hematological system, lymphatic system reticuloendothelial system, nervous system, endocrine and exocrine system, skeletomuscular system including bone, connective tissue, cartilage and skeletal muscle, pulmonary system, gastrointestinal system including the liver, reproductive system, immune system, cardiovascular system, urinary system, auditory or olfactory system;

(4) treating diseases of the cardiovascular system which comprises administering a tetrapyrrolic molecule that coordinates gallium in the central tetrapyrrolic core and irradiating the graft with energy at a wavelength capable of exciting the molecule, so that the graft is made less immunogenic to the host, and

(5) new gallium porphyrin compounds e.g. compounds of formula (IA).

R1, R2 = CO2R3, CON(R4), CONHNH(R4), CON(R4)2, COR4, CON(R4)(R5), (CH2)nOH, (CH2)nOR6, (CH2)n1CO2R7, (CHX)n1CO2R7, (CX2)n1CO2R7, (CH2)n1CONHR8, (CH2)n1CON(R8)2, (CX2)n1CON(R8)R9, (CX2)n1CONHR8, (CX2)n1CON(R8)2, (CX2)n1CON(R8)R9, (CH2)nNHR10, (CH2)nN(R10)2, (CH2)nN(R10)R11, S(R12), (CH2)nS(R13), (CH2)nOPO2OR14, (CH2)nPO(OR14)2, (CH2)nPO2R14, (CH2)nPOR14, (CH2)nNHCOR15, (CH2)nNHCOR15, (CH2)nNHNHCOR15, SO3R16, SO2NHR16, SO2N(R16)2, SO2N(R16)R17, SO2NHNHR16 or SO2R16;

R3, R7 = a counter ion or Q;

Q = 1-20C alkyl or heteroalkyl, aryl or heteroaryl, mono-, di- or poly-hydroxyalkyl, mono-, di- or poly-hydroxyaryl or a functional group of less than 100000 daltons;

R4, R5 = Q, H, mono-, di- or poly-etheralkyl, mono-, di- or poly-etheraryl, amino acid, amino acid ester or amino acid amide;

R6 = alkyl or heteroalkyl, aryl or heteroaryl, mono-, di- or poly-hydroxyalkyl, mono-, di- or poly-hydroxyaryl or a functional group of less than 100000 daltons;

n = 0-4;

n1 = 1-4

X = halo;

R8-R13 = Q, H, mono-, di- or poly-etheralkyl, or mono-, di- or poly-etheraryl;

R14 = H, Q, mono-, di- or poly-etheralkyl, mono-, di- or poly-etheraryl or a counter ion;

R15 = 1-20C alkyl or heteroalkyl, aryl or heteroaryl or a functional group of less than 100000 daltons;

R16, R17 = H, a counter ion, 1-20C alkyl, haloalkyl, heteroalkyl, haloheteroalkyl, aryl or heteroaryl, mono-, di- or poly-hydroxyalkyl, mono-, di- or poly-etheralkyl, mono-, di- or poly-etheraryl, amino acid, amino acid salt, amino acid ester, amino acid amide or a functional group of less than 100000, and

M = Ga3+ with an associated charge balancing counter ion,

provided that:

(1) R4 and R5 are not pentetic acid, polyfunctional carboxy compounds or cyclen functional groups that bind metal ions with atomic numbers of 20-32, 37-39, 42-51 or 57-83;

(2) R12 does not include carboxy, and

(3) R1 and R2 are not both COOH or both CO2Me.

ACTIVITY - Cardiant; Antiarteriosclerotic; Vasotropic; Vulnerary, Antipsoriatic; Immunosuppressive; Antiulcer; Antiinflammatory; Fungicide; Dermatological; Antisebbhoreic; Cytostatic; Virucide; Antibacterial.

Tests are described, but no relevant results are given in the source

material.
MECHANISM OF ACTION - None given in the source material.
USE - Used for treating a vessel (e.g. an artery or a vein) wall or tissue adjoining the vessel wall, or material attached to the vessel wall of a coronary, carotid or peripheral vasculature, for treating or detecting cardiovascular disease (e.g. atherosclerosis, restenosis and graft disease), for treatment of restenosis (e.g. vessel wall negative geometric remodeling, intimal thickening, increased intraluminal shear stress, dysfunctional or absent endothelium, periadventitial fibrosis, increased motor tone, fibrotic contracture and scar formation) of occlusive tissue (e.g. foreign tissue, host tissue, a tissue from an injury via invasive or non-invasive surgical manipulation (such as suturing, vascular access, anastomosis, bypass procedure, or shunt) formation induced in the vessel wall or by vascular injury (e.g. via balloon angioplasty, stent deployment or injury from endovascular device) to the vessel wall; for treatment of arteriovenous shunts and for restructuring the epithelia or endothelial layers of skin and for stopping or arresting hair growth.
The methods are also used for the detection or treatment of tissue such as
atherosclerotic plaque, for the treatment of disturbance of vascular and perivascular cellular processes selected from proliferation, replication, migration, necrosis, apoptosis, adhesion, matrix deposition, signaling pathways, paracrine and autocrine functions, mediator release, contraction, relaxation, shrinkage, phenotype changes, angiogenesis, aggregation, healing, repair, regulation of surrounding tissue, metabolism and matrices and in photodynamic therapy,
MRI diagnosis and radiodiagnostics.
ADVANTAGE - The compounds show good efficacy in advanced animal model systems and preferred uptake in the target tissue, with good clearance characteristics and low toxicity, have good uptake into cardiovascular tissues, show low myocardial tissue toxicity on light activation and are cleared rapidly from skin and other tissues.
Dwg.0/0

L7 ANSWER 284 OF 536 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2001-280428 [29] WPIDS
CR 2001-502594 [49]
DNN N2001-199881 DNC C2001-085006
TI Composition containing bis-indocyanine dye and carrier, useful in diagnosis and therapy, e.g. of tumors, with the dye resistant to aggregation.
DC A96 B04 E23 P31
IN ACHILEFU, S; BUGAJ, J E; DORSHOW, R B; RAJAGOPALAN, R
PA (MLCW) MALLINCKRODT INC
CYC 1
PI US 6183726 B1 20010206 (200129)* 15p
ADT US 6183726 B1 US 2000-484321 20000118
PRAI US 2000-484321 20000118
AB US 6183726 B UPAB: 20011001
NOVELTY - Composition (A) comprises (i) a bis-indocyanine dye (I) with a heterocyclic group in the polymethine chain and (ii) a pharmaceutically acceptable carrier or excipient.
DETAILED DESCRIPTION - Composition (A) comprises (i) a bis-indocyanine dye of formula (I) with a heterocyclic group in the polymethine chain and (ii) a pharmaceutically acceptable carrier or excipient.
a5 = 0-5;
W5, X5 = -CH((CH2)zQ)2;
Q = OH, carboxy or -NRpRz;
z = 0-5;

Rp, Rz = -(CH2)c-COOH, -CH2-(CH2-O-CH2)d-CH2-COOH, -(CH2)g-NR14(CH2)h-COOH or -(CH2)i-NR15-CH2-(CH2-O-CH2)j-CH2-COOH;
Y5, Z5 = -(CH2)c-COOH, -CH2-(CH2-O-CH2)d-CH2-COOH or -(CH2)g-NR14(CH2)h-COOH;
A3 = single bond; and
B3, C3 = O, S, Se, P or NR38; and
D3 = -CR39R40 or CO; or
A3 = double bond; and
B3 = O, S, Se, P or NR38; and
C3 = N or -CR41; and
D3 = -CR42;
R58 - R66 = H, 1-10C alkyl or alkoxy, -CH2-(CH2-O-CH2)c-CH2-OH, -(CH2)d-COOH, -CH2-(CH2-O-CH2)e-CH2-COOH, -(CH2)f-NH2 or -CH2-(CH2-O-CH2)g-CH2-NH2;
c, e, g, h, i = 1-10;
d, f , j = 1-100; and
R43, R44 = H or 1-10C alkyl.

INDEPENDENT CLAIMS are also included for the following: (a) diagnostic and therapeutic methods that involve administering (A) to a human; and (b) method for making (A) by conjugating dyes to peptides or biomolecules by solid phase synthesis.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - None given.

USE - (A) are useful for optical tomographic imaging of organs; monitoring organ function; **coronary** angiography; fluorescent endoscopy; detection, imaging and therapy (**photodynamic** or localized) of tumors; laser-guided surgery (particularly for detecting micrometastases during laparoscopy); and photoacoustic and sonofluorescent methods. A particular application is diagnosis of atherosclerotic plaque and blood clots. Also, measuring the pattern of blood clearance of (A) can be used for diagnosis of tumors and other diseases.

ADVANTAGE - (I) are designed (i) not to aggregate in solution (by preventing intra- and inter-molecular hydrophobic interactions); (ii) to have many attachment sites near to the chromophore, for formation of a dendrimer; (iii) to allow easy conjugation to biomolecules, and (iv) to have a rigid and extended chromophore backbone that enhances the fluorescent quantum yield and extends the absorbance maximum to beyond 800 nm.

Dwg.0/5

L7 ANSWER 375 OF 536 MEDLINE on STN
AN 95361502 MEDLINE
DN 95361502 PubMed ID: 7634806
TI **Methylene blue** increases **myocardial** function in septic shock.
AU Daemen-Gubbels C R; Groeneveld P H; Groeneveld A B; van Kamp G J; Bronsveld W; Thijs L G
CS Department of Internal Medicine, Medical Center Alkmaar, The Netherlands.
SO CRITICAL CARE MEDICINE, (1995 Aug) 23 (8) 1363-70.
Journal code: 0355501. ISSN: 0090-3493.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199509
ED Entered STN: 19950921
Last Updated on STN: 19950921
Entered Medline: 19950914
AB OBJECTIVE: To study whether the circulatory changes of human septic shock are mediated in part by nitric oxide. DESIGN: Open-label, nonrandomized clinical trial on the effects of methylene blue, an inhibitor of nitric oxide action. SETTING: Intensive care unit of a teaching hospital. PATIENTS: Nine consecutive patients with documented septic shock and a

pulmonary artery catheter in place, after initial resuscitation with fluids, sympathomimetics, and mechanical ventilation. INTERVENTIONS: Hemodynamic and metabolic variables were measured before and then 15, 30, 60, and 120 mins after the start of a 20-min infusion of 2 mg/kg of methylene blue. MEASUREMENTS AND MAIN RESULTS: Patients had a hyperdynamic circulation, and methylene blue increased ($p < .01$) mean arterial pressure from 84 +/- 18 to 109 +/- 31 mm Hg and cardiac index from 4.7 +/- 0.9 to 5.6 +/- 1.2 L/min/m2, before and 30 mins after starting the methylene blue infusion, respectively. Cardiac filling pressures did not change. In the same time interval, the subnormal systemic vascular resistance index increased ($p = .09$) and arterial compliance decreased ($p < .05$). Oxygen delivery and oxygen uptake increased ($p < .05$) from 714 +/- 188 to 865 +/- 250 mL/min/m2 and from 160 +/- 39 to 186 +/- 44 mL/min/m2, respectively. Except for heart rate, which increased by 11 +/- 8 beats/min ($p < .01$), variables returned to baseline values at time = 120 mins. CONCLUSIONS: After initial resuscitation from human septic shock, a single dose of **methylene blue** transiently increases mean arterial pressure and oxygen uptake, associated with a decrease in arterial compliance and increases in **myocardial** function and oxygen delivery. Hence, nitric oxide may be a mediator of the circulatory changes of human septic shock.

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L8 13 L7 AND (OZON? OR PEROXID? OR GERANIOL OR TERPINEOL OR CITRONELL OL OR TERPEN? OR ALKENE?)

=> d 1-13 bib hit

L8 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:452931 CAPLUS
DN 138:183352
TI Serum lipid **peroxide** (LPO) level and reference interval in group of health screening population by hemoglobin.bul.methylene blue (Hb.cntdot.MB) method: New clinical and biochemical findings in groups over and under the cut off point of 1.5nmol/mL
AU Maehata, Eisuke; Yano, Masao; Taira, Sukehisa; Hashimoto, Yoko; Shimomura, Koji; Ishizaka, Hiroko; Yamakado, Minoru; Shiba, Teruo; Inoue, Yuzuru; Taniyama, Matsuo; Suzuki, Terutoki; Kawaguchi, Takeshi
CS Department of Central Clinical Laboratory, Mitsui, Memorial Hospital, Japan
SO Igaku to Yakugaku (2002), 47(3), 481-489
CODEN: IGYAEI; ISSN: 0389-3898
PB Shizen Kagakusha
DT Journal
LA Japanese
TI Serum lipid **peroxide** (LPO) level and reference interval in group of health screening population by hemoglobin.bul.methylene blue (Hb.cntdot.MB) method: New clinical and biochemical findings in groups over and under the cut off point of 1.5nmol/mL
AB It has been eight years since we introduced the LPO-measuring kit by a Hb.bul.**methylene blue** (Hb.cntdot.MB) method in the health screening as an **arteriosclerosis** marker. The .XI..+-.2SD value for LPO is found from the population anal. of the health screening examinees during this period to be 0.25-1.88nmol/mL with the cut off value of 1.5nmol/mL. Upon evaluating the desease information hidden in the population, it is shown that LPO is closely related to .gamma.-GTP and TG in the whole range, and to BMI and T-SOD in the normal range. As a conclusion, LPO is evaluated to be a useful marker reflecting the progress of lifestyle habit illness.
ST serum lipid **peroxide** Hb **methylene blue** **arteriosclerosis**
IT **Peroxides**, analysis
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(lipid; serum lipid **peroxide** (LPO) level found in group of health screening population by Hb.bul.methylene blue (Hb.cntdot.MB) method)
IT Lipids, analysis
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**peroxides**; serum lipid **peroxide** (LPO) level found in group of health screening population by Hb.bul.methylene blue (Hb.cntdot.MB) method)
IT Atherosclerosis
Biomarkers (biological responses)
Blood analysis
Diagnosis
Test kits
(serum lipid **peroxide** (LPO) level found in group of health screening population by Hb.bul.methylene blue (Hb.cntdot.MB) method)
IT Hemoglobins
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(serum lipid **peroxide** (LPO) level found in group of health screening population by Hb.bul.methylene blue (Hb.cntdot.MB) method)
IT 61-73-4, Methylene blue
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(serum lipid **peroxide** (LPO) level found in group of health

screening population by Hb.bul.methylene blue (Hb.cntdot.MB) method)

L8 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:243393 CAPLUS
DN 136:258465
TI The contrast of immunohistochemical studies of myocardial fibrinogen and myoglobin in early myocardial ischemia in rats
AU Zhao, Xiaohong; Chen, Xiaorui; Hu, Jun; Qin, Qisheng
CS Department of Forensic Medicine, Tongji Medical College of Huazhong University of Science and Technology, Wuhan, 430030, Peop. Rep. China
SO Legal Medicine (2002), 4(1), 47-51
CODEN: LEGMFI; ISSN: 1344-6223
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB In this study, an animal model of early myocardial ischemia (EMI) was established by ligating the left anterior descending coronary artery of rats. The exptl. animals were divided into five groups according to different intervals of MI (15, 30 min, 1, 2, and 3 h) and one control group. Tissues from the apex of the myocardium and the adjacent myocardium were taken for paraffin sections, followed by hematoxylin-eosin and streptavidin-biotin-**peroxidase** complex (SABC) staining. Results showed that the myoglobin (Mb) depletion and the fibrinogen (Fg) staining increase were detected in the 30 min MI group. The wavy-like increasing extension of the size and the intensity of the Mb depletoin and the Fg staining intensification from the subendocardial to the subepicardial cells were obsd. along with the prolongation of the ischemic period. Both changes had similar patterns and sensitivity, except Fg was less reliable than Mb as it is more easily contaminated by blood. After over-coming blood contamination, the SABC-Fg technique will provide a new method for the diagnosis of EMI.
IT Stains, biological
(chemotoxylin-**eosin** and streptavidin-biotin-**peroxidase** complex; contrast of immunohistochem. studies of **myocardial** fibrinogen and myoglobin in diagnosis of early **myocardial** ischemia in rats)

L8 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:771912 CAPLUS
DN 136:367558
TI Focal enhancement of expression of c-Met/hepatocyte growth factor receptor in the myocardium in human myocardial infarction
AU Sato, Tetsuya; Tani, Yoshinori; Murao, Satoshi; Fujieda, Hiroyuki; Sato, Hirohiko; Matsumoto, Manabu; Takeuchi, Tamotsu; Ohtsuki, Yuji
CS Department of Cardiology, Royal Prince Alfred Hospital, Camperdown, 2050, Australia
SO Cardiovascular Pathology (2001), 10(5), 235-240
CODEN: CATHE8; ISSN: 1054-8807
PB Elsevier Science Inc.
DT Journal
LA English
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB To det. the distribution and expression level of hepatocyte growth factor (HGF) specific receptor, c-Met, in human myocardial infarction. Autopsies of 13 patients who died without heart diseases (control) and 13 patients with a history of myocardial infarction (2 h to 10 yr before death). The harvested **myocardial** tissues were stained with **hematoxylin-eosin** (H&E) and immunohistochem. stained for c-Met expression by the avidin-biotin-horseradish **peroxidase** complex method using an antibody to c-Met. C-Met expression was only slightly increased in control subjects and in noninfarcted myocardium of

the test group. In contrast, high expression was noted in the peripheral region of the myocardial infarction and in some hypertrophic myocardial cells. C-Met was not expressed in the infarcted myocardium, but overexpression was noted in the surrounding myocardial cells of blood vessels and in the subendocardium and subepicardium in a band-like pattern. The expression level of c-Met was most enhanced at the time of appearance of coagulative necrosis and least in the myocardium of subjects with old infarcts. These results indicate that HGF preferentially reaches the ischemic regions of the myocardium and has local and direct effects on the myocardium in patients with myocardial infarction.

L8 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:865295 CAPLUS
DN 123:336390
TI The involvement of low-density lipoprotein in hemin transport potentiates **peroxidative** damage
AU Miller, Yury I.; Felikman, Yana; Shaklai, Nurith
CS Sackler Institute of Molecular Medicine, Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel
SO Biochimica et Biophysica Acta (1995), 1272(2), 119-27
CODEN: BBACAQ; ISSN: 0006-3002
PB Elsevier
DT Journal
LA English
TI The involvement of low-density lipoprotein in hemin transport potentiates **peroxidative** damage
IT Antioxidants
Biological transport
Blood
Cell membrane
Erythrocyte
Peroxidation
(hemin may be transported from the human RBC membrane to plasma proteins via LDL, which in turn oxidizes LDL)
IT **Arteriosclerosis**
(atherosclerosis, **hemin** may be transported from the human RBC membrane to plasma proteins via LDL, which in turn oxidizes LDL)

L8 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:282389 CAPLUS
DN 122:126646
TI Oxidative crosslinking of LDL protein induced by hemin: involvement of tyrosines
AU Miller, Yury I.; Shaklai, Nurith
CS Sackler Institute Mol. Medicine, Sackler Faculty Medicine, Tel-Aviv University, Tel-Aviv, 698887, Israel
SO Biochemistry and Molecular Biology International (1994), 34(6), 1121-9
CODEN: BMBIES; ISSN: 1039-9712
PB Academic
DT Journal
LA English
AB This study investigated free hemin induced modifications in low d. lipoprotein (LDL). By use of fluorescent probes hemin was found to assoc. with LDL thereby inducing **peroxidn**. of both lipids and protein. Upon LDL **peroxidn**., covalent crosslinking of apolipoprotein B (Apo B) occurred as judged by SDS-PAGE. Concomitantly, a multifluorophore emission developed, which included contribution of bityrosines. The simultaneous formation of protein aggregates and bityrosines was interpreted as the involvement of intermol. bityrosines in the hemin induced crosslinking of Apo B. Since LDL protein aggregation relates to conversion of macrophages into foam cells, hemin should be considered as an endogenous trigger of atherosclerosis.
IT **Peroxidation**
(oxidative crosslinking of human low-d. lipoprotein induced by hemin

and involvement of tyrosines)
IT **Arteriosclerosis**
(atherosclerosis, oxidative crosslinking of human low-d. lipoprotein induced by **hemin** and involvement of tyrosines)

L8 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1994:267221 CAPLUS
DN 120:267221
TI Polyamines mediate coronary transcapillary macromolecular transport in the calcium paradox
AU Trout, Jerome J.; Lu, Chung Y.; Goldstone, Alfred D.; Iqbal, Zafar; Hoenig, Harold
CS Lakeside Med. Cent., Northwestern Univ., Chicago, IL, 60611, USA
SO Journal of Molecular and Cellular Cardiology (1994), 26(3), 369-77
CODEN: JMCDAY; ISSN: 0022-2828
DT Journal
LA English
AB This study addresses the role of polyamines and their rate limiting enzyme, ornithine decarboxylase in regulation of macromol. transport of two macromols., **fluorescein** and horseradish **peroxidase**, across **coronary** capillaries. Rat hearts were isolated and retrogradely perfused through the aorta (Langendorff method), stabilized by 10 min perfusion with Krebs-Henseleit medium contg. Ca2+, followed by 5 min perfusion with Krebs-Henseleit medium without Ca2+ and an addnl. 30 s to 2 min with Krebs-Henseleit medium contg. 1 mg/mL horseradish **peroxidase**. .alpha.-Difluoromethylornithine, the only known function of which is inhibition of ornithine decarboxylase, and putrescine were added as needed. Perfusion with Krevs-Henseleit medium without Ca2+ caused a 2-fold increase in fluorescein transport but a decrease in horseradish **peroxidase** transport. Reperfusion with Krebs-Henseleit medium caused an 4-fold increase in fluorescein transport and a 10-fold increase in horseradish **peroxidase** pos. intraendothelial cell vesicles over control values. .alpha.-Difluoromethylornithine inhibited these increases and putrescine negated the .alpha.-difluoromethylornithine effect. Other morphol. measures of horseradish **peroxidase** transport and assocd. membrane activities including modulation of endothelial cells luminal and abluminal pits were effected in the same manner. Transport of macromols. through coronary capillaries, over the short term studied, appears to be regulated by the ornithine decarboxylase/polyamine pathway.

L8 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1993:99352 CAPLUS
DN 118:99352
TI Measurement of lipid **peroxide** levels in erythrocyte ghosts from patients with various diseases
AU Yoshimine, Noboru; Tateishi, Tohru; Ando, Fujiko; Kuzuya, Fumio
CS Sch. Med., Nagoya Univ., Nagoya, 466, Japan
SO Journal of Clinical Biochemistry and Nutrition (1992), 12(2), 115-20
CODEN: JCBNER; ISSN: 0912-0009
DT Journal
LA English
TI Measurement of lipid **peroxide** levels in erythrocyte ghosts from patients with various diseases
AB By the method using a **methylene blue** deriv., the hydroperoxide (LPO) level of erythrocyte membranes (EG) was investigated in patients suffering from diabetes mellitus, hypertension, cerebral stroke, hypercholesterolemia, and ischemic **heart disease**. In addn., the correlation between the ED-LPO level and the clin. parameters was analyzed. The EG-LPO level registered .apprx.1.6 nmol/mg protein in the healthy controls, whereas higher EG-LPO levels were obtained in the diabetic and the hypertensive patients. However, the EG-LPO in the hypercholesterolemic patients showed lower value than that in the diabetic, suggesting the inhibitory effect of high cholesterol on

lipid **peroxidn**. There was no correlation between the EG-LPO level and the clin. parameters. The lipid **peroxide** in the erythrocyte membrane would be one of the independent vascular risk factors, and esp. the high values of the EG-LPO in the diabetic and hypertensive patients might be related to the high incidence of vascular accidents in these diseases.

ST lipid **peroxide** erythrocyte vasculature disease

IT Diabetes mellitus
Hypertension
(lipid **peroxides** in erythrocytes in, in humans)

IT Erythrocyte
(lipid **peroxides** of, in diabetes and hypertension and cerebral stroke and hypercholesterolemia and ischemic heart disease in humans)

IT Heart, disease
(ischemia, lipid **peroxides** in erythrocytes in, in humans)

IT Lipids, compounds
RL: BIOL (Biological study)
(**peroxides**, of erythrocyte membranes, in diabetes and hypertension and cerebral stroke and hypercholesterolemia and ischemic heart disease in humans)

IT Brain, disease
(stroke, lipid **peroxides** in erythrocytes in, in humans)

IT 57-88-5, Cholesterol, biological studies
RL: BIOL (Biological study)
(metabolic disorders, hypercholesterolemia, lipid **peroxides** in erythrocytes in, in humans)

L8 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1992:123418 CAPLUS

DN 116:123418

TI **Peroxidative** crosslinking of myosins

AU Bhoite-Solomon, V.; Kessler-Icekson, G.; Shaklai, N.

CS Sackler Fac. Med., Tel Aviv Univ., Israel

SO Biochemistry International (1992), 26(1), 181-9
CODEN: BIINDF; ISSN: 0158-5231

DT Journal

LA English

TI **Peroxidative** crosslinking of myosins

ST myosin crosslinking hemin heart muscle; myoglobin **peroxidn** crosslinking hemin heart muscle; **peroxidn** crosslinking myosin heart muscle; heart disease damage myosin **peroxidn** crosslinking

IT Myoglobins
RL: BIOL (Biological study)
(myosin of heart and skeletal muscle **peroxidative** crosslinking by, in hydrogen **peroxide** presence and absence)

IT Heart, toxic chemical and physical damage
Heart, disease
(myosin **peroxidative** crosslinking by myoglobin and **hemin** and hydrogen **peroxide** in model of)

IT Myosins
RL: RCT (Reactant); RACT (Reactant or reagent)
(**peroxidative** crosslinking of, of heart and skeletal muscle by hemin and myoglobin and hydrogen **peroxide**)

IT Crosslinking
(**peroxidative**, of myosin, of heart and skeletal muscle by hemin and myoglobin and hydrogen **peroxide**)

IT Bond formation
(sulfur-sulfur, in myosin of heart and skeletal muscle **peroxidative** crosslinking by hemin and myoglobin, hydrogen **peroxide** in relation to)

IT Heart, composition
(ventricle, myosin of, **peroxidative** crosslinking of, by myoglobin and hemin and hydrogen **peroxide**)

IT 7722-84-1, Hydrogen **peroxide**, biological studies
RL: BIOL (Biological study)
(myosin of heart and skeletal muscle **peroxidative** crosslinking by, hemin and myoglobin in relation to)
IT 16009-13-5, Hemin
RL: BIOL (Biological study)
(myosin of heart and skeletal muscle **peroxidative** crosslinking by, in hydrogen **peroxide** presence and absence)

L8 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1992:122794 CAPLUS
DN 116:122794
TI Hydrogen **peroxide**-induced pulmonary vasodilation: role of guanosine 3',5'-cyclic monophosphate
AU Burke-Wolin, Theresa; Abate, Charles J.; Wolin, Michael S.; Gurtner, Gail H.
CS Dep. Med., New York Med. Coll., Valhalla, NY, 10595, USA
SO American Journal of Physiology (1991), 261(6, Pt. 1), L393-L398
CODEN: AJPHAP; ISSN: 0002-9513
DT Journal
LA English
TI Hydrogen **peroxide**-induced pulmonary vasodilation: role of guanosine 3',5'-cyclic monophosphate
AB H2O2, but not tert-Bu hydroperoxide, produces a concn.-dependent vasodilation of the pulmonary circulation in isolated saline perfused rabbit lungs when pulmonary arterial pressures (PAP) are raised with the thromboxane analog U-46619. This vasodilation was enhanced in the presence of indomethacin, suggesting that H2O2 possesses both a prostaglandin-mediated constrictor and an addnl. dilator mechanism. In isolated rabbit intrapulmonary arteries the endothelium did not alter the dose-dependent relaxation of arterial rings to H2O2, and indomethacin enhanced the relaxant response of the **peroxide**. The decrease in PAP and relaxation of isolated pulmonary **arteries** obsd. with H2O2 was attenuated with 10 .mu.M **methylene blue**, an inhibitor of sol. guanylate cyclase activation. M & B 22948, a cGMP-selective phosphodiesterase inhibitor, enhanced the vasodilation or relaxation to the **peroxide** in both prepns. These changes were not endothelium dependent. Inhibition of the cGMP-assocd. endothelium-derived relaxant factor (EDRF) with nitro-L-arginine, did not alter relaxation of arterial rings to **peroxide**. Thus, H2O2 appears to produce pulmonary vasodilation through the activation of guanylate cyclase and accumulation of cGMP. Both H2O2 and EDRF may function as tonic stimulators of guanylate cyclase in the pulmonary circulation and contribute to the maintenance of low basal pressures.
ST hydrogen **peroxide** pulmonary vasodilation cGMP
IT Prostaglandins
RL: BIOL (Biological study)
(hydrogen **peroxide** effect on pulmonary circulation in relation to)
IT Circulation
(pulmonary, hydrogen **peroxide** effect on, cGMP in relation to)
IT Artery
(pulmonary, endothelium, hydrogen **peroxide** effect on, cGMP in relation to)
IT 7665-99-8, CGMP 9054-75-5, Guanylate cyclase
RL: BIOL (Biological study)
(hydrogen **peroxide** effect on pulmonary circulation in relation to)
IT 75-91-2, tert-Butyl hydroperoxide
RL: BIOL (Biological study)
(pulmonary circulation in response to, hydrogen **peroxide** in relation to)
IT 7722-84-1, Hydrogen **peroxide**, biological studies
RL: BIOL (Biological study)

(pulmonary circulation response to, cGMP in relation to)

L8 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1989:151917 CAPLUS
DN 110:151917
TI Hydrogen **peroxide** and cGMP may function as an oxygen sensor in the pulmonary artery
AU Burke-Wolin, Theresa; Wolin, Michael S.
CS Dep. Physiol., New York Med. Coll., Valhalla, NY, 10595, USA
SO Journal of Applied Physiology (1989), 66(1), 167-70
CODEN: JAPHEV; ISSN: 8750-7587
DT Journal
LA English
TI Hydrogen **peroxide** and cGMP may function as an oxygen sensor in the pulmonary artery
AB The effects of O tension on force in precontracted isolated pulmonary arterial smooth muscle from calf lungs was characterized to investigate the mechanism of O tension sensing. These **arteries** display a decrease in force with increasing O tension that is antagonized via inhibition of sol. guanylate cyclase activation by 10 .mu.M **methylene blue** or inactivation of catalase by pretreatment with 50 mM 3-amino-1,2,4-triazole for 30 min. O tension-dependent relaxation is assocd. with an increase in intracellular H2O2 metab. through catalase (detected as the **peroxide**-dependent inactivation of tissue catalase activity by aminotriazole) and cGMP, known mediators of relaxation in calf pulmonary arteries. Thus, a recently reconstructed mechanism of activation of sol. guanylate cyclase involving the metab. of H2O2 by catalase appears to function as an O tension sensor in pulmonary arteries.
ST lung artery oxygen sensor; cGMP lung artery oxygen sensor; hydrogen **peroxide** lung artery oxygen sensor
IT Artery
(contraction-relaxation of, oxygen sensor system for, hydrogen **peroxide** and cGMP in)
IT 7722-84-1, Hydrogen **peroxide**, biological studies
RL: BIOL (Biological study)
(-cGMP system, as oxygen sensor in regulation of pulmonary artery contraction-relaxation)
IT 7665-99-8, CGMP
RL: BIOL (Biological study)
(-hydrogen **peroxide** system, in regulation of pulmonary artery contraction-relaxation)
IT 9054-75-5, Guanylate cyclase
RL: PROC (Process)
(activation of, by hydrogen **peroxide** metab. by catalase, as oxygen sensor system in regulation of pulmonary artery contraction-relaxation)
IT 9001-05-2, Catalase
RL: BIOL (Biological study)
(hydrogen **peroxide** metab. by, guanylate cyclase activation by, as oxygen sensor system in regulation of pulmonary artery contraction-relaxation)
IT 7782-44-7, Oxygen, biological studies
RL: BIOL (Biological study)
(hydrogen **peroxide**-cGMP system in pulmonary artery as sensor for, in regulation of contraction-relaxation)

L8 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1988:49061 CAPLUS
DN 108:49061
TI Flunarizine reduces cerebral infarct size after photochemically induced thrombosis in spontaneously hypertensive rats
AU Van Reempts, J.; Van Deuren, B.; Van de Ven, M.; Cornelissen, F.; Borgers, M.

CS Dep. Life Sci., Janssen Pharm. Beerse, Beerse, B-2340, Belg.
SO Stroke (1987), 18(6), 1113-19
CODEN: SJCCA7; ISSN: 0039-2499
DT Journal
LA English
AB The cerebroprotective effect of flunarizine was studied in a minimally invasive model of photochem. induced cerebral infarction in spontaneously hypertensive rats. I.v. administration of the photosensitizing dye **rose bengal** and intense focal illumination of the brain produced a deep cortical **infarction** that resulted from singlet oxygen-induced **peroxidative** injury to the endothelial membrane, subsequent platelet adhesion, and eventual thrombus formation. The infarct size was calcd. from area measurements on consecutive histol. sections prepd. from the brain cortex 4 h after the onset of the insult. Oral treatment with 40 mg/kg flunarizine 3 h before photoexcitation resulted in a significant redn. of the median infarct size from 11.75 mm3 in the untreated group to 6.40 mm3 in the treated group. At this dose, flunarizine had no effect on systemic blood pressure. In a sep. expt. the area of thrombotic obstruction was quantified 30 min after the onset of light exposure. Flunarizine did not significantly reduce early thrombus formation (2.28 mm3 in the untreated and 1.78 mm3 in the treated group). The infarcted area at 4 h was considerably larger than the initial thrombotic area. Protection with flunarizine against development of cortical infarction has been unequivocally shown. Although some effect may already be present at the early stage of lesion formation, the major protective action admittedly occurred in the later postinsult period when the lesion was expanding. The obsd. beneficial effects may be attributed to preservation of the integrity of endothelial cell membranes (redn. of platelet adhesion and vasogenic edema formation), of neuronal cell membranes (inhibition of toxic Ca2+ overload), and of glial cell membranes (prevention of cytotoxic edema formation). The results indicate that flunarizine may be of clin. use for the suppression of thrombotic stroke.

L8 ANSWER 12 OF 13 MEDLINE on STN
AN 94307003 MEDLINE
DN 94307003 PubMed ID: 8033657
TI The significance of endothelial injury in the pathogenesis of coronary heart disease.
AU Yang L X; Zhu S J
CS Department of Cardiology, Xinqiao Hospital, Third Military Medical University, Chongqing.
SO CHUNG-HUA NEI KO TSA CHIH CHINESE JOURNAL OF INTERNAL MEDICINE, (1993 Dec) 32 (12) 816-8.
Journal code: 16210490R. ISSN: 0578-1426.
CY China
DT Journal; Article; (JOURNAL ARTICLE)
LA Chinese
FS Priority Journals
EM 199408
ED Entered STN: 19940825
Last Updated on STN: 19940825
Entered Medline: 19940817
AB In this study, the number of circulating endothelial cells (CEC) was counted and used as an indicator of the injury of vascular endothelial cells (VEC) in 27 cases with **coronary heart disease** (CHD), in vivo, CECs were identified with **fluorescein**-labeled anti-human antibody to factor VIII related antigen. The contents of MDA representing lipid **peroxides** were also measured in these cases. Meanwhile the number of CEC in normal people was counted as control and compared with that in patients before and after therapy. The results were as follows: The number of CEC and content of MDA in the patients were higher than that in normal people and these two induces were significantly correlated (r = 0.802). The CEC number reflects the severity of CHD. The present investigation suggests

that VEC injury induced by the lipid **peroxide** may play an important role in the pathogenesis of the CHD and CEC counting can be used as a reference for judging the severity and the prognosis of the CHD.

CT Check Tags: Female; Human; Male
Aged
Cell Count
Coronary Disease: BL, blood
*Coronary Disease: ET, etiology
*Endothelium, Vascular: PA, pathology
English Abstract
Lipid Peroxidation
Malondialdehyde: BL, blood
Middle Age

L8 ANSWER 13 OF 13 MEDLINE on STN
AN 90372164 MEDLINE
DN 90372164 PubMed ID: 2396514
TI Morphological changes in acute cerebral ischemia after occlusion and reperfusion in the rat.
AU Nakagawa Y; Fujimoto N; Matsumoto K; Cervos-Navarro J
CS Department of Neurosurgery, National Kagawa Children's Hospital, Japan.
SO ADVANCES IN NEUROLOGY, (1990) 52 21-7.
Journal code: 0367524. ISSN: 0091-3952.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199010
ED Entered STN: 19901109
Last Updated on STN: 19980206
Entered Medline: 19901011

AB Blood-brain barrier permeability was investigated in acute focal ischemia after MCA occlusion and reperfusion. Four kind of tracers were used: sodium fluorescein and ionic lanthanum as a small molecular tracer, and Evans blue and HRP as a macromolecular tracer. BBB permeability to the tracers was observed macroscopically and studied by electron microscopy. The MCA was dissected free and occluded by ligation with 10-0 monofilament nylon suture. In the reperfusion model, the nylon suture was cut and the occluded MCA was reopened. Diffuse fluorescein staining was noted in the ipsilateral cortex; however, there was no extravasation of Evans blue or HRP in the occlusion model. Ionic lanthanum was demonstrated in the interendothelial space, basement membrane, and extracellular space. In the reperfusion model, intense **fluorescein** staining and hemorrhagic **infarction** were observed. Remarkable extravasation of Evans blue and HRP was also revealed in the ischemic lesion. HRP was demonstrated in the basement membrane and around the neuropils. Ultrastructural findings suggested that small molecules such as sodium fluorescein and ionic lanthanum may pass through the entire interendothelial cleft into the extracellular space before leakage of the macromolecules in the acute ischemic stage. Between 30 to 60 min after MCA occlusion, cerebral edema may begin with an escape of water and ions through the tight junctions. Reperfusion of MCA in the acute stage of ischemia may lead to abnormal vascular permeability to macromolecules as a manifestation of severe damage to the BBB.

CT Check Tags: Animal; Comparative Study; Female; Male
Acute Disease
*Blood-Brain Barrier
Brain Edema: ME, metabolism
*Brain Edema: PA, pathology
Evans Blue: PK, pharmacokinetics
Fluorescein
Fluoresceins: PK, pharmacokinetics
Horseradish Peroxidase: PK, pharmacokinetics
Lanthanum: PK, pharmacokinetics

Microscopy, Electron
Molecular Weight
Particle Size
Pinocytosis
Rats
Rats, Inbred Strains
Reperfusion
CN 0 (Fluoresceins); EC 1.11.1.- (Horseradish **Peroxidase**)